I hereby certify that, on the date shown below, this correspondence is being:
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Date: October 14, 2002 By: _____
Lois Miller

PATENT

Atty. Docket No. DX0804K

CN 028008

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: PARHAM, et al.	Examiner: Sandra L. Wegert
Serial No.: 09/265,540	Art Unit: 1646
Filed: March 8, 1999	**DECLARATION UNDER 37 C.F.R. 1.132**
For: POLYNUCLEOTIDES ENCODING DIRS1 (as amended)	Palo Alto, California 94304
	October 11, 2002

DECLARATION UNDER 37 C.F.R. §1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Honorable Sir:

I, Edward P. Bowman hereby declare that:

1. I received my Ph.D. degree from Emory University in 1994. I have extensive experience in the area of immunology, as evidenced by my authorship of 15 research publications in the field of mammalian immunology, as described in my attached curriculum vitae.

2. I have read and understood that the present invention relates to DIRS1, which is identified as a subunit of IL-20 receptor, a receptor that mediates skin inflammation, and shows significant homology to human interferon-γ (IFN-γ) receptor beta subunit and to receptors signaling through the JAK receptor.

3. I have read the Examiner's rejections of Claims 16 and 21-25 as presented in the latest Office action, dated August 12, 2002. I understand that the Examiner has maintained one rejection of these claims based on a lack of a specific, substantial, or credible utility, as described in the Manual of Patent Examining Procedure §§2107-2107.03 (MPEP, 8th ed., August 2001).

4. The present application contains a number of asserted utilities that are substantial, specific, and credible, e.g., "means to modulate the effect of a cytokine upon binding to its receptor, and therefore potentially useful in treating inappropriate immune response, e.g., autoimmune, inflammation . . . to inhibit the receptor . . .," and use in diagnosis (page 2, lines 35-37, to page 3, line 3, and page 55, lines 4-5 of Specification).

5. Data generated after the priority date of the present application confirm the asserted utility noted above. Page 68, lines 29-36, to page 69, lines 1-10, of the specification generically describe expression of DISR1 in various tissues and cell lines. Southern blot data generated after the priority date demonstrate that DIRS1 expression is significantly increase in psoriatic skin tissue relative to normal skin tissue. DIRS1 expression was higher in LPS treated dendritic cells while expression in resting dendritic cells was significantly lower. No detectable signal was found in normal colon, ulcerative colitis colon, normal thyroid, and Hashimoto's thyroiditis.

6. In view of the increased expression in psoriatic skin and activated dendritic cells (which are known to be a mediator of psoriasis, see, e.g., Nestle, et al. (1994) J. Clin. Invest. 94:202-209; and Mitra, et al. (1995) J. Immunol. 154:2668-2677), one skilled in the art would believe that these data confirm the asserted utility of treating inflammation, e.g., of psoriasis, by inhibiting DIRS1. Also confirmed is the use of this receptor in a diagnostic context to assess expression of DIRS1 in an inflammatory disorder.

7. Based on the foregoing, one of ordinary skill in the art would believe the asserted utility of DIRS1 as a diagnostic or as a therapeutic target as being substantial, specific, and credible.

8. I hereby attest that I do not have any financial interest in the present application, U.S. Ser. No. 09/265,540, filed March 8, 1999, Attorney Docket DX0804K.

9. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and, that these statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: October 11, 2002

By: _____
Edward P. Bowman, Ph.D.

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Attachment: Curriculum vitae of Dr. Edward P. Bowman

EDWARD PAUL BOWMAN, Ph.D.

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EDUCATION

Ph.D. 1994 Department of Biochemistry, Emory University, Atlanta, GA
Thesis: A Small GTP-Binding Protein Regulates Neutrophil Phospholipase D
Advisor: J. David Lambeth M.D., Ph.D.

B.S. 1988 Department of Chemistry, N. Carolina State University, Raleigh, NC

PROFESSIONAL EXPERIENCE

DNAX Research Institute, Palo Alto, CA, 2000-present

Associate Principle Scientist- Supervised three research associates' efforts involved in achieving the research goals of the chemokine program. Identification and characterization of anti-human CCR10 and anti-mouse CXCR3 monoclonal antibodies. Development of a high-throughput competent CCR10 cell line. Determination of CCR10 expression by blood leukocytes and the homing receptor and cytokine secretion profiles of CCR10+ CD4 T-cells. Extended the studies of CCR10+ cells to leukocytes from psoriasis and atopic dermatitis donors. Facilitated the acquisition of human disease skin sample to allow EPP's discovery of disease-associated genes in psoriasis and atopic dermatitis.

Established mouse models of skin graft rejection and intradermal SEB induced T-cell inflammation to study the role of CTACK in T-cell mediated skin disease. Established a mouse model of wound healing to investigate the role of and the potential application of novel DNAX molecules or antagonists of novel DNAX molecules during human wound healing.

Stanford University, Laboratory of Eugene Butcher, M.D., 1994-2000

Postdoctoral Fellow- Developed a transient transfection system for lymphocytes to allow the study of signal transduction pathways required for lymphocyte chemotaxis and adhesion. Examined RGS (regulator of G-protein signaling) family members' modulation of lymphocyte chemotaxis and adhesion stimulated by various chemokines and classical chemoattractants. These experiments were the first to investigate the potential of RGS modulation of leukocyte homing to normal lymph nodes and inflamed tissue. These results identify additional targets for small molecule inhibitor development that would regulate leukocyte homing.

Investigated the ability of isolated mouse lymphocyte subsets to respond to a previously known chemokines using a more sensitive assay developed in this laboratory. Have discovered previously unrecognized chemokine:lymphocyte subset interactions that identify additional targets that regulate lymphocyte migration within secondary lymphoid tissues. These targets would be attractive candidates for small molecule inhibitor development to control inappropriate inflammatory conditions.

Emory University, Laboratory of J. David Lambeth, M.D., Ph.D., 1988-1994
Graduate Student- Examined the intracellular regulation of human neutrophil phospholipase D. Determined that rho small GTP-binding proteins were required for GTPγS-stimulated phospholipase D activity in neutrophil lysates. Expressed recombinant small GTP-binding protein guanine nucleotide exchange factors and demonstrated their ability to modulate rho-dependent GTPγS-stimulated phospholipase D activity. Partially purified a cytosolic factor that was required for neutrophil phospholipase D activity. This work was the first to demonstrate that small GTP-binding proteins regulated lipid-dependent signal transduction pathways. These results were one of the first of many reports that identified multiple downstream targets of the rho family of small GTP-binding proteins.

Glaxo-Wellcome (Burroughs-Wellcome), Laboratory of Ken Bair, Ph.D., 1985-1987
Cooperative Education Student- Isolated natural plant products to be further modified by organic synthesis to produce cancer therapeutic agents. This work contributed to a compound that progressed to Phase I clinical trials.

AWARDS

Arthritis Foundation Postdoctoral Fellowship	1996-1999
NIH Postdoctoral Training Grant	1994-1996
NIH Predoctoral Training Grant	1990-1992

PUBLICATIONS

1. Kunkel, E.J., Kim, C.H., Genovese, M.C., Vierra, M.A., Soler, D., **Bowman, E.P.**, and Butcher E.C. CCR10 Expression on IgA Antibody Secreting Cells: A Unifying Feature of the Human Mucosal Secretory IgA Immune System (in preparation)

2. Wright, D.E., **Bowman, E.P.**, Wagers, A.J., Butcher, E.C., and Weissman, I.L. Hematopoietic Stem Cells are Uniquely Selective in their Migratory Response to Chemokines. (submitted)

3. Hudak, S., Hagen, M., Catron, D., Oldham, E., McEvoy, L., and **Bowman, E.P.**, Immune surveillance and effector functions of CCR10+ skin homing T-cells. (submitted).
4. Riviere, C., Geay, G.F., Leonardi, M., Foudi, A., **Bowman, E.P.**, Vainchenker, W., and Louache, F. Expression of Regulators of G protein Signalling (RGS) proteins during megakaryocytic differentiation: role in CXCR4 signaling. (submitted).
5. Homey, B., Alenius, H., Muller, A., Soto, H., **Bowman, E.P.**, Yuan, W., McEvoy, L., Lauerma, A.I., Assmann, T., Bunemann, E., Lehto, M., Wolff, H., Yen, D., Marxhausen, H., To, W., Sedgwick, J., Ruzick,a T., Lehmann, P., Zlotnik, A. CCL27--CCR10 interactions regulate T cell--mediated skin inflammation. *Nat Med.* 8(2):157-65 (2002).
6. **Bowman, E.P.**, Kuklin, N.A., Youngman, K.R., Lazarus, N.H., Kunkel, E.J., Pan, J., Greenberg, H.B., and Butcher, E.C. The Intestinal Chemokine Thymus-expressed Chemokine (CCL25) Attracts IgA Antibody-secreting Cells. *Journal of Experimental Medicine*.195:269-275 (2002).
7. **Bowman, E.P.**, Campbell, J.J., Soler, D., Dong, Z., Manlongat, N., Picarella, D., Hardy, R.R. and Butcher, E.C. Developmental Switches in Chemokine Response Profiles during B-cell differentiation and maturation. *Journal of Experimental Medicine*. 191:1303-1317 (2000).
8. **Bowman, E.P.**, Campbell, J.J., Druey, K.M., Scheschonka, A., Kehrl, J.H., and Butcher, E.C. Regulation of Chemotactic and Proadhesive Responses to Chemoattractant Receptors by RGS Family Members. *Journal of Biological Chemistry*. 273: 28040-28048 (1998).
9. Campbell, J.J., **Bowman E.P.**, Murphy, K., Youngman, K.R., Siani M.A., Thompson, D.A., Wu, L., Zlotnik, A. and Butcher, E.C. 6-C-kine (SLC), a Lymphocyte Adhesion-triggering Chemokine Expressed by High Endothelium, Is an Agonist for the MIP-3β Receptor CCR7. *Journal of Cell Biology*. 141: 1053-1059 (1998).
10. **Bowman, E.P.**, Uhlinger, D.J., and Lambeth, J.D. Neutrophil Phospholipase D: Inhibition by Rho GDI and Stimulation by smg GDS. *Methods in Enzymology*. 256: 246-256 (1995).
11. Lambeth, J.D., Kwak, J.Y., **Bowman, E.P.**, Perry, D., Uhlinger, D.J., and Lopez, I. ADP Ribosylation Factor functions synergistically with a 50 kDa cytosolic factor in cell-free activation of human neutrophil phospholipase D. *Journal of Biological Chemistry*. 270: 2431-2434 (1995).
12. **Bowman, E.P.**, Uhlinger, D.J., and Lambeth, J.D. Neutrophil Phospholipase D is Activated by a Membrane-Associated Rho Family Small Molecular Weight GTP-Binding Protein. *Journal of Biological Chemistry*. 268: 21509-21512 (1993).
13. Olson, S.C., **Bowman, E.P.**, and Lambeth, J.D. Phospholipase D Activation in a Cell-free System from Human Neutrophils by Phorbol 12-Acetate and Guanosine 5′-O-(3-Thiotriphosphate): Activation is Calcium Dependent and Requires Protein Factors in Both the Plasma Membrane and Cytosol. *Journal of Biological Chemistry*. 266:17236-17242 (1991).

14. Xu, T.S., **Bowman, E.P.**, and Lambeth, J.D. Stimulation of Adrenal Mitochondrial Cholesterol Side-Chain Cleavage by GTP, Steroidogenesis Activator Polypeptide (SAP) and Steroid Carrier Protein 2: GTP and SAP act Synergistically. *Journal of Biological Chemistry*. 266: 6801-6807 (1991).
15. Glass, D.B., Robertson, D.G., Xu, T.S., **Bowman, E.P.**, and Lambeth, J.D. Chemical Synthesis, Initial Conformational Studies, and Activity of Rat Steroidogenesis Activator Peptide and a Truncated Analog. *Endocrine Research*. 17: 307-326 (1990).